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| 09/287,377      | 04/07/1999  | ROBERT J. D'AMATO    | 05213-0272          | 6240             |

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EXAMINER

JONES, DWAYNE C

ART UNIT PAPER NUMBER

1614

DATE MAILED: 09/24/2003

27

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/287,377

Applicant(s)

D'AMATO, ROBERT J.

Examiner

Dwayne C Jones

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 June 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 7-12, 15, 19-39 and 43-48 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 7, 9, 12, 15, 19, 20, 26-39 and 45-48 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Status of Claims***

1. Claims 7-12, 15, 19-39, and 43-48 are pending.
2. Claims 7, 9, 12, 15, 19, 20, 26-39, and 45-48 are rejected.

### ***Response to Arguments***

3. Applicant's arguments, see Paper No 26, filed June 11, 2003, with respect to the rejection(s) of claim(s) 7-12, 15, 19-39, and 43-48 under Billson et al. in view of Little, II have been fully considered and are persuasive regarding the angiogenesis inhibiting compound of thalidomide. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Billson et al. in view of Little, II. for claim 9 when the angiogenesis inhibitory composition is represented by the compounds P), Q), R), and S).

### ***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 15, 19, 20, 26-39, and 45-48 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time

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the application was filed, had possession of the claimed invention. There is insufficient descriptive support for the phrases "inhibiting angiogenesis" and "treating angiogenesis dependent disease". In addition, the instant specification does not describe what is meant by the phrases "inhibiting angiogenesis" and "treating angiogenesis dependent disease" other than the diseases of corneal neovascularization and Crohn's Disease. Structural identifying characteristics of the phrases "inhibiting angiogenesis" and "treating angiogenesis dependent disease" are not disclosed except for those the diseases of corneal neovascularization and Crohn's Disease. There is no evidence that there is any per se structure/function relationship between the phrases "inhibiting angiogenesis" and "treating angiogenesis dependent disease" other than those disclosed, namely the diseases of corneal neovascularization and Crohn's Disease. The instant specification does provide an adequate written description for the phrases "inhibiting angiogenesis" and "treating angiogenesis dependent disease". Accordingly, these claims fail to comply with the written description requirement.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 9 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 9 and 12 are rejected as failing to define the invention in the manner required by 35 U.S.C. 112, second paragraph. The claims must be in one sentence form only.

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9. Claims 7, 26, and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons support this rejection. The variables of  $R_8$  and  $R_{11}$  are defined as a quaternary nitrogen atom,  $N^+$ . The variable of X is  $R_{25}C(=O)C(CH_2)_nC(=O)R_{26}$  has incomplete valency with the attached carbon atom. Accordingly, these anomalies render the claim vague and indefinite.

***Claim Rejections - 35 USC § 103***

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. Claims 7-12, 15, 19-39 and 43-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Billson et al. of WO 95/03807. Billson et al. teach of treating an inflammatory response in the macula of the eye, namely age-related macular degeneration, with the administration of anti-inflammatory agent, (see abstract). Billson

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et al. teach that of an example of an anti-inflammatory agent that of steroids, (see pages 2 and 3). The skilled artisan would have been motivated from the teachings of Billson et al. to utilize other types of agents which possess the pharmacological property of inhibiting inflammation. Moreover, the prior art reference of Billson et al. disclose that the anti-inflammatory agents can be practiced alone or in conjunction with other therapies or agents, (see page 4, lines 1-4). Billson et al. teach the skilled artisan that other substances, such as anti-angiogenesis agents, can be added to the anti-inflammatory agent. Billson et al. state that amongst the various types of anti-inflammatory agents that may be utilized, a variety of anti-angiogenesis agents can be combined in a composition. As an illustration of an anti-angiogenesis agent, Billson et al. provide the example of thalidomide, (see page 4, lines 1-4 and claims 1, 2, 5 and 11-13). With this information provided from Billson et al., one having ordinary skill in the art is provided with the motivation to utilize any agent that is an angiogenesis agent, which would obviously embrace thalidomide as well as its derivatives and analogues. In addition, it is well established in the art that angiogenesis is the formation of new blood vessels into a tissue or organ. It is also well documented that unregulated angiogenesis occurs in numerous disease states and conditions which are associated or dependent on angiogenesis, (for instance, see the instant section entitled Background of the Invention, pages 1-7 of this application). Accordingly, it would be obvious to the skilled artisan to treat these various disease states or conditions with angiogenesis inhibitors. Due to the fact that Billson et al. teach of the combined administration of an anti-inflammatory compound with an anti-angiogenesis agent, one having ordinary skill in

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the art would be motivated to treat a variety of conditions and ailments in which angiogenesis is unregulated. Furthermore, Billson et al. disclose that the steroid of triamcinolone acetonide is used to treat macular degeneration, (see page 4, lines 11-19). The determination of the mode, method and dosage of the administration of these pharmaceuticals is well within the purview of the skilled artisan. Clearly, one having ordinary skill in the art is provided with the motivation to utilize an anti-inflammatory agent along with that of anti-angiogenesis agent from the teachings and support from Billson et al. In addition, the skilled artisan would have been motivated to utilize and substitute other agents, as well as their respective derivatives and analogues, to just as long as they maintain the pharmaceutical properties of being known as anti-inflammatory agents as well as anti-angiogenesis agents. For these reasons, the instant invention is rendered obvious over the prior art reference of Billson et al.

13. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Billson et al. of WO 95/03807 in view of Little, II et al of U.S. Patent No. 5,348,942. Billson et al. teach of treating an inflammatory response in the macula of the eye, namely age-related macular degeneration, with the administration of anti-inflammatory agent, (see abstract). Billson et al. teach that of an example of an anti-inflammatory agent that of steroids, (see pages 2 and 3). The skilled artisan would have been motivated from the teachings of Billson et al. to utilize other types of agents which possess the pharmacological property of inhibiting inflammation. Moreover, the prior art reference of Billson et al. disclose that the anti-inflammatory agents can be practiced alone or in conjunction with other therapies or agents, (see page 4, lines 1-4). Billson et al. teach the skilled artisan

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that other substances, such as anti-angiogenesis agents, can be added to the anti-inflammatory agent. Billson et al. state that amongst the various types of anti-inflammatory agents that may be utilized, a variety of anti-angiogenesis agents can be combined in a composition. As an illustration of an anti-angiogenesis agent, Billson et al. provide the example of thalidomide, (see page 4, lines 1-4 and claims 1, 2, 5 and 11-13). With this information provided from Billson et al., one having ordinary skill in the art is provided with the motivation to utilize any agent that is an angiogenesis agent, which would obviously embrace thalidomide as well as its derivatives and analogues. In addition, it is well established in the art that angiogenesis closely associated with endothelial cell proliferation and constitutes the development of new capillary blood vessels.

14. Angiogenesis is also associated with a variety of pathological conditions in which it would be desirable to inhibit such new blood vessel development, inter alia, the growth of tumors, diabetic retinopathy, retrolental fibroplasias, neovascular glaucoma, psoriasis, rheumatoid arthritis, hemangiomas, Kaposi's sarcoma, (see column 2, lines 14-38 of Little, II et al.). Accordingly, it would obvious to the skilled artisan to treat these various disease states or conditions with angiogenesis inhibitors, as suggested by Billson et al. and Little, II et al. Due to the fact that Billson et al. teach of the combined administration of an anti-inflammatory compound with an anti-angiogenesis agent, one having ordinary skill in the art would be motivated to treat a variety of conditions and ailments in which angiogenesis is unregulated. Furthermore, Billson et al. disclose that the steroid of triamcinolone acetonide is used to treat macular degeneration, (see page



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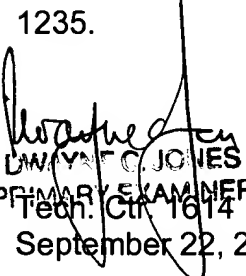
4, lines 11-19). The determination of the mode, method and dosage of the administration of these pharmaceuticals is well within the purview of the skilled artisan. Clearly, one having ordinary skill in the art is provided with the motivation to utilize an anti-inflammatory agent along with an anti-angiogenesis agent from the teachings and support from Billson et al. and Little, II et al. In addition, the skilled artisan would have been motivated to utilize and substitute other agents, as well as their respective derivatives and analogues, to just as long as they maintain the pharmaceutical properties of being known as anti-inflammatory agents as well as anti-angiogenesis agents. In particular when the angiogenesis inhibitory composition is represented by the compounds P), Q), R), and S) in claim 9 the above stated-rejected renders the instant invention obvious for the following reasons even though claim 7 has the proviso of excluding the compound of thalidomide. It would have been obvious to the skilled artisan that thalidomide can easily be made via internal cyclization reactions for the compounds P), Q), R), and S) in claim 9. Accordingly, because the prior art reference of Billson et al. specifically teach of thalidomide, the skilled artisan would have been motivated to use thalidomide precursor compounds as elucidated by compounds P), Q), R), and S) in claim 9 due to the fact that they only vary from thalidomide via an internal cyclization reaction.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. C. Jones whose telephone number is (703) 308-4634. The examiner can normally be reached on Mondays through Fridays from 8:30 am to 6:00 pm. The examiner can also be reached on alternate Mondays.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on (703) 308-4725. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

  
DAVID C. JONES  
PRIMARY EXAMINER  
Tech. Ctr. 1614  
September 22, 2003